PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 08 August 2000 (08.08.00)	
International application No. PCT/CA99/01194	**Applicant's or agent's file reference** 1038-998 MIS
International filing date (day/month/year) 16 December 1999 (16.12.99)	**Priority date** (day/month/year) 17 December 1998 (17.12.98)
Applicant CATES, George, A. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

10 July 2000 (10.07.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Claudio Borton
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

RECEIVED APR 24 2001

CLAIMS

What we claim is:

1. A multivalent immunogenic composition for conferring protection in a host against disease caused by infection by respiratory syncytial virus (RSV) and influenza virus, which comprises:

(a) an immunoeffective amount of a mixture of purified fusion (F) protein, attachment (G) protein and matrix (M) protein of RSV, and

(b) an immunoeffective amount of a non-virulent influenza virus preparation.

2. The immunogenic composition of claim 1 formulated as a vaccine for *in vivo* administration to the host wherein the individual components (a) and (b) of the composition are formulated such that the immunogenicity of the individual components (a) and (b) is not impaired.

3. The immunogenic composition of claim 2 further comprising an adjuvant.

4. The immunogenic composition of claim 3 wherein said adjuvant imparts an enhanced immune response to RSV when compared to the mixture (a) formulated with the adjuvant in the absence of the non-virulent influenza virus preparation.

5. The immunogenic composition of claim 3 wherein the adjuvant is poly-di(carboxylatophenoxy)-phosphazene (PCPP).

6. The immunogenic composition of claim 1 wherein said mixture (a) is present in an amount of about 10 to about 200 μg and (b) is present in an amount of about 1 to about 100 μg, in a single dose.

7. The immunogenic composition of claim 1 wherein said fusion (F) protein comprises multimeric fusion (F) proteins.

8. The immunogenic composition of claim 7 wherein, when analyzed under non-reducing conditions, said multimeric fusion (F) protein includes heterodimers of molecular weight approximately 70 kDa and dimeric and trimeric forms.

9. The immunogenic composition of claim 1 wherein, when analyzed under non-reducing conditions, said attachment (G) protein comprises G protein of

molecular weight approximately 95 kDa and G protein of molecular weight approximately 55 kDa and oligomeric G protein.

10. The immunogenic composition of claim 1 wherein, when analyzed by SDS-PAGE under non-reducing conditions, said matrix (M) protein comprises M protein of molecular weight approximately 28 to 34 kDa.

11. The immunogenic composition of claim 1 wherein, when analyzed by reduced SDS-PAGE analysis, said fusion (F) protein comprises an F_1 subunit of molecular weight approximately 48 kDa and an F_2 subunit of molecular weight approximately 23 kDa, said attachment (G) protein comprises a G protein of molecular weight approximately 95 kDa and a G protein of molecular weight approximately 55 kDa, and said matrix (M) protein comprises an M protein of approximately 31 kDa.

12. The immunogenic composition of claim 1 wherein said F, G and M proteins are present in mixture (a) in the relative proportions of:

F from about 35 to about 70 wt%

G from about 5 to about 30 wt%

M from about 10 to about 50 wt%

13. The immunogenic composition of claim 12 wherein, when analyzed by SDS-PAGE under reducing conditions and silver stained, the ratio of F_1 subunit of molecular weight approximately 48 kDa to F_2 subunit of molecular weight approximately 23 kDa is between 1:1 to about 2:1 as determined by scanning densitometry.

14. The immunogenic composition of claim 13 wherein said mixture is at least about 75% pure.

15. The immunogenic composition of claim 1 wherein said RSV proteins in said mixture are from one or both of subtypes RSV A and RSV B.

16. The immunogenic composition of claim 1 wherein said non-virulent influenza virus preparation comprises a plurality of different non-virulent influenza virus strains.

17. The immunogenic composition of claim 16 wherein said non-virulent influenza virus preparation is an inactivated influenza virus preparation.

18. The immunogenic composition of claim 16 wherein said non-virulent infleunza virus preparation comprises an attenuated influenza virus.

19. The immunogenic composition of claim 1 wherein said non-virulent influenza virus preparation comprises at least one influenza antigen.

20. The immunogenic composition of claim 1 when used as a vaccine.

21. A method of immunizing a human host against disease caused by infection by respiratory syncytial virus (RSV) and by influenza virus, which comprises administering to the host an immunoeffective amount of the immunogenic composition of claim 1.

22. The method of claim 21 wherein said immunogenic composition is formulated as a vaccine for *in vivo* administration to the host wherein the individual components (a) and (b) of the composition are formulated such that the immunogenicity of the individual components (a) and (b) is not impaired.

23. The method of claim 22 wherein said host is a human host of at least 18 years of age.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
1038-998 MIS		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/CA 99/ 01194	16/12/1999	17/12/1998
Applicant		
CONNAUGHT LABORATORIES LIMITED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [X] None of the figures.

PATENT COOPERATION TREATY

PCT

REC'D 09 MAR 2001
WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
1038-998 MIS		

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA99/01194	16/12/1999	17/12/1998

International Patent Classification (IPC) or national classification and IPC
A61K39/295

Applicant
CONNAUGHT LABORATORIES LIMITED et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
10/07/2000	06.03.2001

Name and mailing address of the international preliminary examining authority:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Herrero, M

Telephone No. +49 89 2399 8542

INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

International application No. PCT/CA99/01194

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-23	as originally filed				

Claims, No.:

1-21	as received on	05/01/2001	with letter of	27/12/2000	

Drawings, sheets:

1/5-5/5	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 20 and 21 with respect to industrial applicability.

because:

☒ the said international application, or the said claims Nos. 20 and 21 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-21

	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-21
Industrial applicability (IA)	Yes:	Claims	1-19
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

SECTION III

Claims 20 and 21 relate to medical uses considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

SECTION V

2. CITATIONS AND EXPLANATIONS

2.1 The following document has been considered for the purposes of this report:

D1: WO 98/02457 (also cited in the application)

Document D1, which is considered to represent the most relevant state of the art, discloses immunogenic compositions that may be formulated as a vaccine, which contain an immunoeffective amount of the F, G and M proteins of respiratory syncytial virus (RSV), and at least one additional immunogen such as from influenza (*emphasis added*), which may be incorporated into the compositions as polyvalent (combination) vaccines (see the paragraph bridging pages 7-8 and the passage on page 15, lines 33-36 bridging over page 16, lines 1-6).

2.2 The arguments put forward by the Applicants in their letter dated 27.12.00, in reply to the written opinion dated 29.09.00, as well as the enclosures therein have been taken into consideration.

The subject-matter of the newly filed Claims 1 to 21 may now be regarded as formally novel over the relevant disclosures of D1 (see above). Thus, present Claims 1 to 21 would appear to meet the requirements of Art. 33(2) PCT.

However, it is not apparent on which grounds present Claims 1 to 21 should be regarded as inventive. In spite of the Applicants explanations, the teachings of D1 (see above) still appear to render obvious the subject-matter hereby claimed.

The technical problem underlying the present application relates to the provision of a multivalent immunogenic composition suitable for conferring protection in a host against disease caused by infection by RSV and influenza virus.

In order to solve the problem posed the present disclosure proposes the combination of (a) an immunoeffective amount of a mixture of purified fusion (F) protein, attachment (G) protein and matrix (M) protein of RSV and (b) an immunoeffective amount of a non-virulent influenza virus preparation.

According to the description a "surprising effect" associated with the hereby proposed combination of the aforementioned components (a) + (b) should be seen in the fact that, in the resulting multivalent immunogenic composition, no apparent detrimental effect in the immunogenicity of the individual components is detected, i.e. the combined vaccine formulation provides an immune response in the host which is substantially the same as the response obtained by administration of the components individually.

At the moment, no suitable evidence is available on the basis of which it should be assumed that, according to the general knowledge in the field, it would have been normally expected that the direct combination of **the particular components (a) + (b) in a single formulation** would have resulted in a detrimental effect on the immunogenicity of (any of) the individual components. Conversely, the corresponding teachings in the closest prior art D1 (see the paragraph bridging pages 7-8, which exemplifies 13 possible pathogen sources for the additional immunogen one of them being influenza) have to be seen both as a positive indication of the feasibility of the resulting immunogenic compositions and as an incentive to the skilled person to further develop the suggested polyvalent combination vaccines.

For this reason it is considered that, in order to provide a multivalent immunogenic composition suitable for conferring protection in a host against disease caused by infection by RSV and influenza virus, the skilled person, who did not have to overcome any technical prejudice, would have turned, at the relevant date of the present application, to the closest prior art document D1. In this way, according to

the straightforward indications found in D1, the skilled person would have arrived at a solution to the problem posed equivalent to the one hereby claimed, without having to exercise any inventive activity. In this regard, the fact that the present claims require that the influenza immunogen be a non-virulent influenza virus preparation, e.g. an influenza virus preparation rendered non-virulent by inactivation with formaldehyde (see page 8, lines 10-12 or page 11, lines 13-14), can only be seen as a matter of obvious choice, vis-à-vis the intended protective purposes of the resulting vaccine formulations.

Thus, contrary to the requirements of Article 33(3) PCT, no inventive contribution is recognisable in claiming the multivalent immunogenic compositions encompassed by present Claim 1, either as such (Claim 1) or when used as a vaccine (Claim 19). The same objection (Art. 33(3) PCT) applies to the method of immunizing a human host according to present Claim 20.

Dependent Claims 2-18 and 21 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, as in the present technical context the preferred embodiments therein contemplated merely represent the choice of additional desirable vaccine components (Claims 2-4) or administration conditions (Claim 21), nature (Claims 6-10) and relative proportions (Claims 11-14) of the sub-components in respect of the (a) component, which had been already described in D1 (see page 5, lines 23-35 bridging over page 6, lines 1-32), component ratios which in principle do not appear to result in any advantageous effect (Claim 5) or well known possible working options in respect of the (b) component (Claims 15-18), all of which would have come within the scope of the customary practice followed by persons skilled in the art.

2.3 Industrial applicability (Art. 33(4) PCT)

For the assessment of the present Claims 1-19 and 20-21 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but

may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

SECTION VII

The expression "herein incorporated by reference" in respect of prior art documents on page 1, lines 10-11; page 6, lines 10-11 and 14-15; page 7, lines 26-27 and page 15, line 14 leads to a doubt as to whether the requirements of the description being self-contained are satisfied (see PCT Guidelines C-II, 4-17).

SECTION VIII

1. Claim 1 does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claim attempts to define the multivalent immunogenic compositions of interest in terms of the result to be achieved, which merely amounts to a statement of the underlying problem. The functional characterization "... wherein the individual components (a) and (b) of the composition are formulated such that the immunogenicity of the individual components (a) and (b) is not impaired" does not enable the skilled person to determine which technical features are necessary to perform the stated functions.

   The technical features necessary for achieving this intended result, i.e. the actual relative quantities of components (a) and (b) required to obtain an effective composition (e.g. those referred to in Example 4), should have been added.

   The above deficiency affects *mutatis mutandis* the subject-matter of the claims dependent thereon (Claims 2-4, 6-10, 14-19) and appended thereto (Claims 20-21) respectively.

2. An additional objection equivalent to the foregoing (Art. 6 PCT) has to be raised against Claim 3, in which the constituting adjuvant of interest is also defined making use of relative functional terms.

CLAIMS

What we claim is:

1. A multivalent immunogenic composition for conferring protection in a host against disease caused by infection by respiratory syncydial virus (RSV) and influenza virus, which comprises:

(a) an immunoeffective amount of a mixture of purified fusion (F) protein, attachment (G) protein and matrix (M) protein of RSV, and

(b) an immunoeffective amount of a non-virulent influenza virus preparation.

said immunogenic composition of being formulated as a vaccine for *in vivo* administration to the host wherein the individual components (a) and (b) of the composition are formulated such that the immunogenicity of the individual components (a) and (b) is not impaired.

2. The immunogenic composition of claim 1 further comprising an adjuvant.

3. The immunogenic composition of claim 2 wherein said adjuvant imparts an enhanced immune response to RSV when compared to the mixture (a) formulated with the adjuvant in the absence of the non-virulent influenza virus preparation.

4. The immunogenic composition of claim 2 wherein the adjuvant is poly-di(carboxylatophenoxy)-phosphazene (PCPP).

5. The immunogenic composition of claim 1 wherein said mixture (a) is present in an amount of about 10 to about 200 μg and (b) is present in an amount of about 1 to about 100 μg. in a single dose.

6. The immunogenic composition of claim 1 wherein said fusion (F) protein comprises multimeric fusion (F) proteins.

7. The immunogenic composition of claim 6 wherein, when analyzed under non-reducing conditions, said multimeric fusion (F) protein includes heterodimers of molecular weight approximately 70 kDa and dimeric and trimeric forms.

8. The immunogenic composition of claim 1 wherein, when analyzed under non-reducing conditions, said attachment (G) protein comprises G protein of molecular weight approximately 95 kDa and G protein of molecular weight approximately 55 kDa and oligomeric G protein.

9. The immunogenic composition of claim 1 wherein, when analyzed by SDS-PAGE under non-reducing conditions, said matrix (M) protein comprises M protein of molecular weight approximately 28 to 34 kDa.

10. The immunogenic composition of claim 1 wherein, when analyzed by reduced SDS-PAGE analysis, said fusion (F) protein comprises an F_1 subunit of molecular weight approximately 48 kDa and an F_2 subunit of molecular weight approximately 23 kDa, said attachment (G) protein comprises a G protein of molecular weight approximately 95 kDa and a G protein of molecular weight approximately 55 kDa, and said matrix (M) protein comprises an M protein of approximately 31 kDa.

11. The immunogenic composition of claim 1 wherein said F, G and M proteins are present in mixture (a) in the relative proportions of:

F from about 35 to about 70 wt%

G from about 5 to about 30 wt%

M from about 10 to about 50 wt%

12. The immunogenic composition of claim 11 wherein, when analyzed by SDS-PAGE under reducing conditions and silver stained, the ratio of F_1 subunit of molecular weight approximately 48 kDa to F_2 subunit of molecular weight approximately 23 kDa is between 1:1 to about 2:1 as determined by scanning densitometry.

13. The immunogenic composition of claim 12 wherein said mixture is at least about 75% pure.

14. The immunogenic composition of claim 1 wherein said RSV proteins in said mixture are from one or both of subtypes RSV A and RSV B.

15. The immunogenic composition of claim 1 wherein said non-virulent influenza virus preparation comprises a plurality of different non-virulent influenza virus strains.

16. The immunogenic composition of claim 15 wherein said non-virulent influenza virus preparation is an inactivated influenza virus preparation.

17. The immunogenic composition of claim 15 wherein said non-virulent influenza virus preparation comprises an attenuated influenza virus.

18. The immunogenic composition of claim 1 wherein said non-virulent influenza virus preparation comprises at least one influenza antigen.

19. The immunogenic composition of claim 1 when used as a vaccine.

20. A method of immunizing a human host against disease caused by infection by respiratory syncytial virus (RSV) and by influenza virus, which comprises administering to the host an immunoeffective amount of the immunogenic composition of claim 1.

21. The method of claim 20 wherein said host is a human host of at least 18 years of age.

PATENT COOPERATION TREATY

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SIM & McBURNEY
SIM, HUGHES, ASHTON & McKAY

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Stewart,Michael,T.
Sim & McBurney
330 University Avenue
6th Floor
Suite 600
Toronto, Ontario M5G 1R7
CANADA

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	06.03.2001
Applicant's or agent's file reference: 1038-998 MIS	IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA99/01194	16/12/1999	17/12/1998

Applicant
CONNAUGHT LABORATORIES LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Papiol Rovira, M Tel.+49 89 2399-7199

Form PCT/IPEA/416 (July 1992)

[redacted]ENT COOPERATION TREATY [redacted]

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

To:
Sim & McBurney
Attn. Stewart,Michael,T.
330 University Avenue
6th Floor
Toronto, Ontario M5G 1R7
CANADA

Date of mailing *(day/month/year)*	27/07/2000
Applicant's or agent's file reference: 1038-998 MIS	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No.: PCT/CA 99/ 01194	International filing date *(day/month/year)* 16/12/1999

Applicant

CONNAUGHT LABORATORIES LIMITED et al.

1. [X] The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

[ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

[ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Catherine Humbert

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
1038-998 MIS		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/CA 99/ 01194	16/12/1999	17/12/1998
Applicant		
CONNAUGHT LABORATORIES LIMITED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [X] None of the figures.

PCT

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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A3

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09/213,770 17 December 1998 (17.12.98) US

(71) Applicant *(for all designated States except US)*: CONNAUGHT LABORATORIES LIMITED [CA/CA]; 1755 Steeles Avenue, Toronto, Ontario M2R 3T4 (CA).

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(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
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(88) Date of publication of the international search report:
26 October 2000 (26.10.00)

(54) Title: MULTIVALENT IMMUNOGENIC COMPOSITION CONTAINING RSV SUBUNIT COMPOSITION AND INFLUENZA VIRUS PREPARATION

(57) Abstract

Immunogenic compositions for administration to adults, particularly to the elderly, to protect them against disease caused by infection by respiratory syncytial virus and by influenza virus comprise an immunoeffective amount of a mixture of purified fusion (F) protein, attachment (G) protein and matrix (M) protein of RSV and an immunoeffective amount of a non–virulent influenza virus preparation. The components of the composition, when formulated as a vaccine for *in vivo* administration, do not impair the immunogenicity of each other. The immunogenic composition may also contain an adjuvant.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/[redacted] 99/01194

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K39/295 A61P31/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
BIOSIS, CHEM ABS Data, WPI Data, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 02457 A (CONNAUGHT LABORATORIES) 22 January 1998 (1998-01-22) the whole document	1-23
Y	WO 96 33738 A (VOLVOVITZ) 31 October 1996 (1996-10-31) examples 1,5	1-23
A	WO 95 34308 A (CONNAUGHT LABORATORIES) 21 December 1995 (1995-12-21) cited in the application the whole document	3,4
A	US 5 494 673 A (ANDRIANOV) 27 February 1996 (1996-02-27) examples 6,9	5

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
20 July 2000	27/07/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Skelly, J

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/AU 99/01194

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		WO 9502416 A	26-01-1995
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INTERNATION[redacted]SEARCH REPORT

International application No.
[redacted]PCT/CA 99/01194

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 21-23 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/07109

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D217/18 C07D217/04 C07D217/20 C07D223/16 C07D209/44
C07D401/04 C07D401/06 C07D401/12 C07D405/04 A61K31/472
A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 21656 A (PFIZER ;CAMERON KIMBERLY O (US); JARDINE PAUL A DASILVA (US); ROSA) 18 July 1996 (1996-07-18) cited in the application claims	1-44
A	WO 92 18498 A (PFIZER) 29 October 1992 (1992-10-29) claims	1-44
A	EP 0 842 661 A (PFIZER) 20 May 1998 (1998-05-20) claims	1-44

☐ Further documents are listed in the continuation of box C.

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 July 2000	27/07/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Chouly, J

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/07109

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